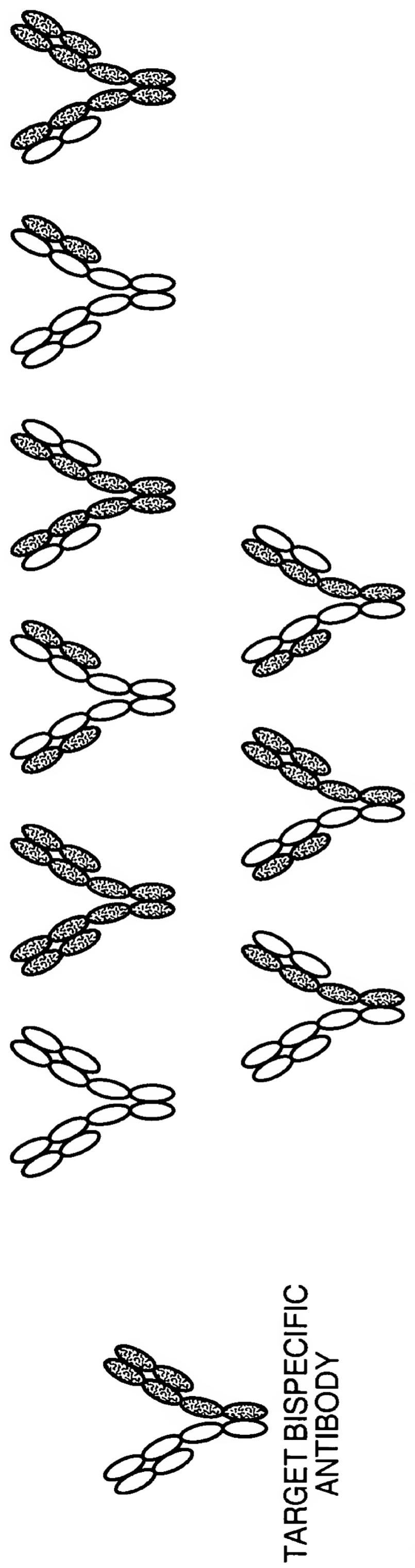


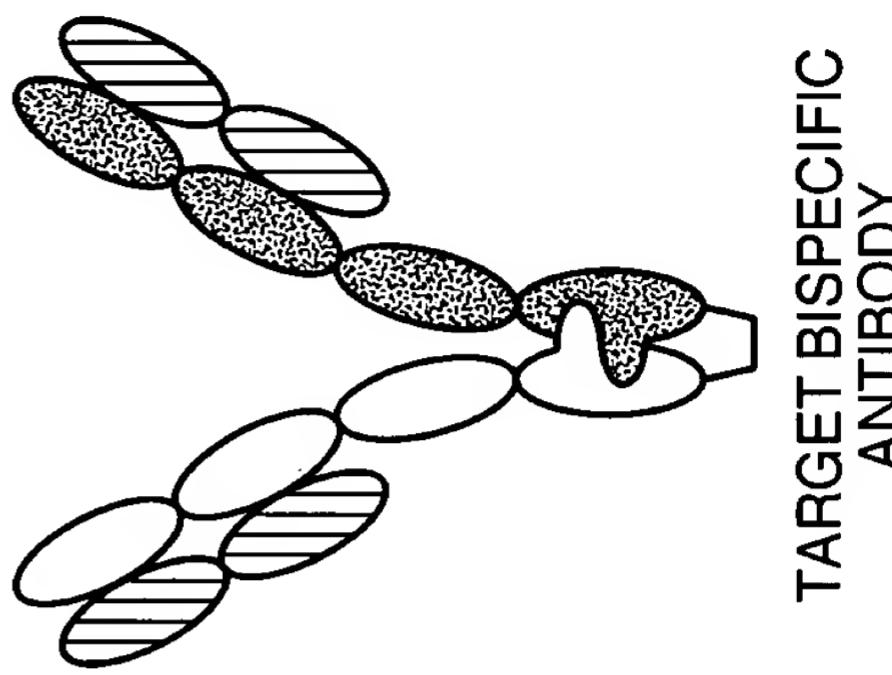


Heller Ehrman LLP
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Docket No.: 39766-0215C1
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POSSIBLE CONTAMINATING SPECIES

FIG. 1A



TARGET BISPECIFIC ANTIBODY

POSSIBLE MAJOR CONTAMINATING SPECIES

TARGET BISPECIFIC ANTIBODY

U = ENGINEERED DISULFIDE BOND BETWEEN C_H3 DOMAINS

FIG. 1B

FIG. 1C

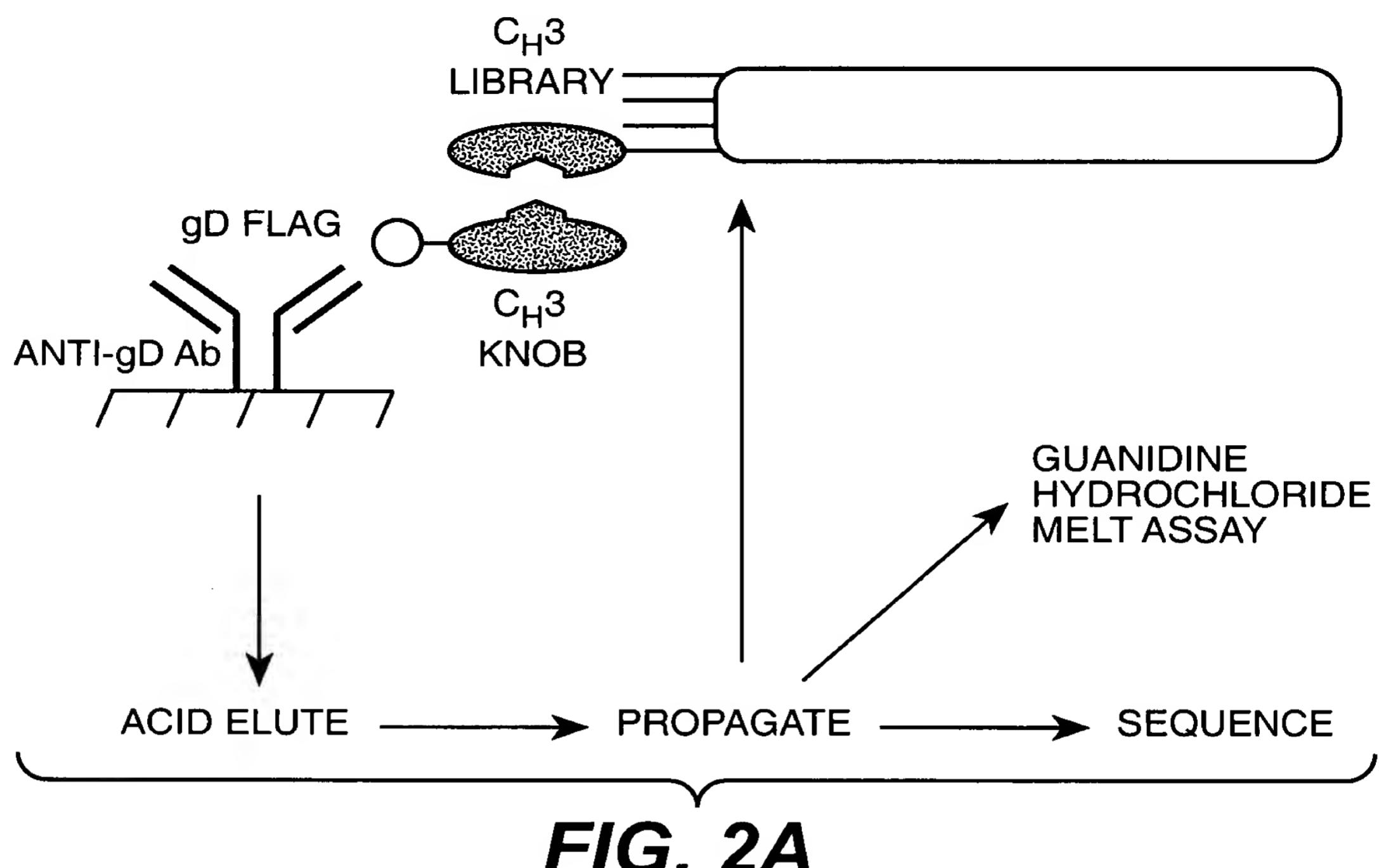


FIG. 2A



FIG. 2B

FIG. 2C-1

FIG. 2C

FIG. 2C-2

stII -> gd flag -> G site -> CH3
N A Y A L K M A D P N R F R G K D L A A H Y G Q P
AACGGTTACGCTTGAAAATGGCGAACCGAACCCGTTTCGTGGTAAGATCTGGCTGCACACTACGGCCAGGCC
MluI 75

R E P Q V Y T L P P S R E E M T K N Q V S L W C L
CGGGAACCTCAGGTGTATAACCCTGCCACCGTCTCGAGAAATGACTAAAACCAGGTCTCTGTGGTGCCTG
150

350 360 366
V K G F Y P S D I A V E W E S N G Q P E N N Y K T
GTCAAAGGTTCTATCCGAGCGATATGCCGTGGAATGGGAAAGCAACGGTCAAAACAAACTACAAACCC
225

370 380 390
T P P V L D S D G S F F L Y S K L T V D K S R W Q
ACTCCACCGGTGGATTCTGATGGCTCCTCTGTGACCAAGCCGTTGACA
400 410
300

420 Q G N V F S C S V M H E A L M N H Y T Q K S L S L
CAAGGCCAACGTTTCAGCTGTCTGTTATGCACGAGGCCACTACACCCAGAAAAGCCTGTCCTG
375
S P G K O
TCTCCCCGGAAATAAGGCTGAGGCTCCTAGAGGTTGAGGTGATTTTATGAAAAAGAATATCGCATTTCTTCTTG
450
M K K N I A F L L
→ stII
440
350
A S M F V F S I A T N A Y A G Q P R E P Q V Y T L
CATCTATGTTCGTTCTATTGCTACAAACGGGTACGGCTGGCTGGGAGGGAGAACCGTGTACACCCTG
525
→ CH3
5 360 366 368 370
P P S R E E M T K N Q V S L Y C L V K G F Y P S D
CCCCATCCCCGGAAAGGAGATGACCAAGAACCCAGGTAAAGCTTGTACTGCCCTGTTCAAAGGCTTCTATCCCAGCGACA
HindIII
600
380 390 400
I A V E W E S N G Q P E N N Y K T T P P V L D S D
TCGCCGTGGAGTGGAGGAATGGGCAGCCGGAGAACACTACAAGACCCACGGCTCCCGTGTGGACTCCGACCG
675
407 410 420
G S F F L Y S F L T V D K S R W Q Q G N V F S C S
GCTCCTTCCCTCACAGCTTCTCACCGTGTGACAAAGAGGCAGGGCAGGGAAACGTCTCATGCTCCG
SalI
750
430 440
V M H E A L H N H Y T Q K S L S P G K Am G P
TGATGCATGAGGCTCTGGCACAAACCAACTACACGGAGGCTCTCCCTGTCTCGGGTAATAAGGGCCCC (SEQ ID NO: 13)
Apal

FIG. 2C-2

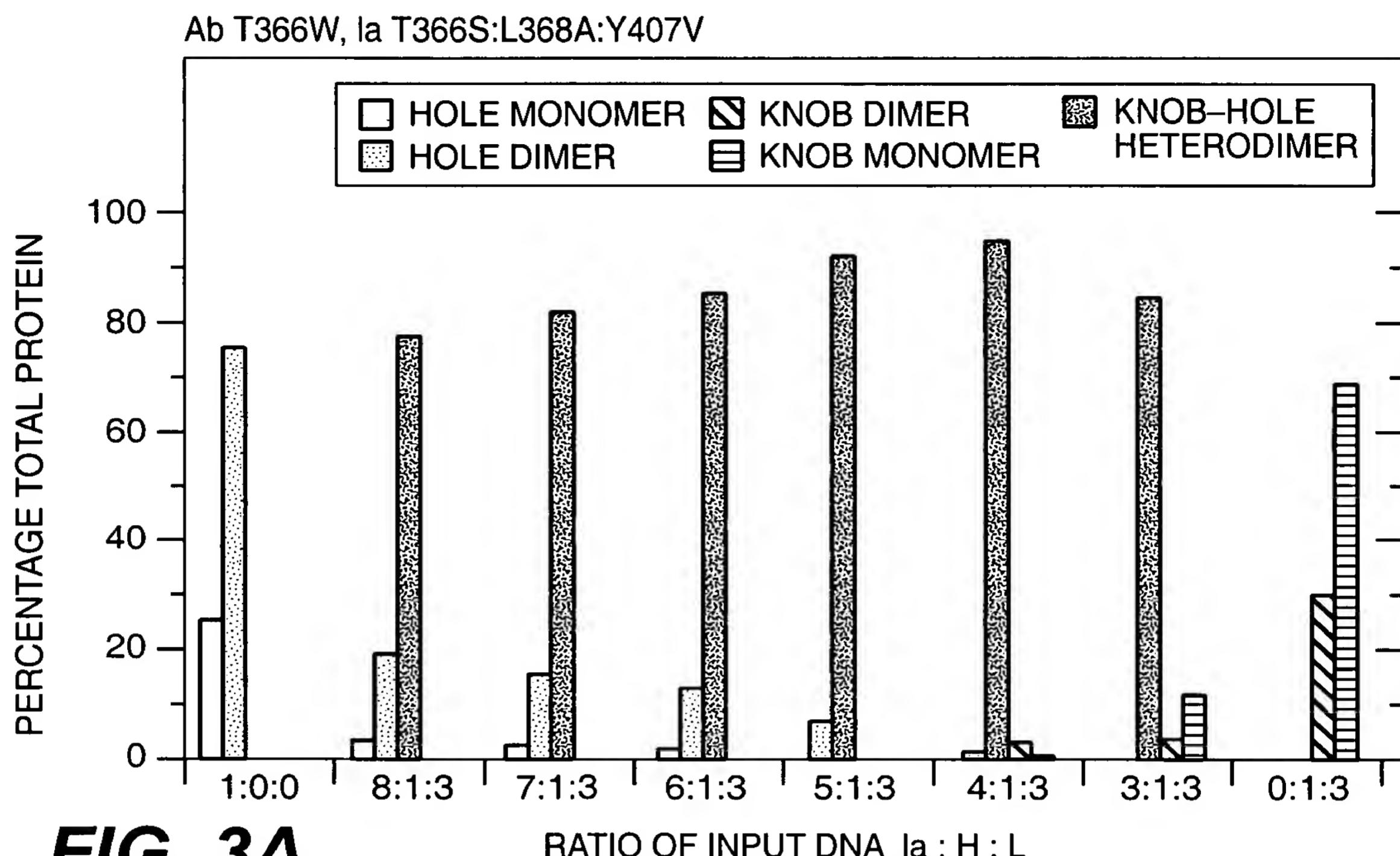


FIG. 3A

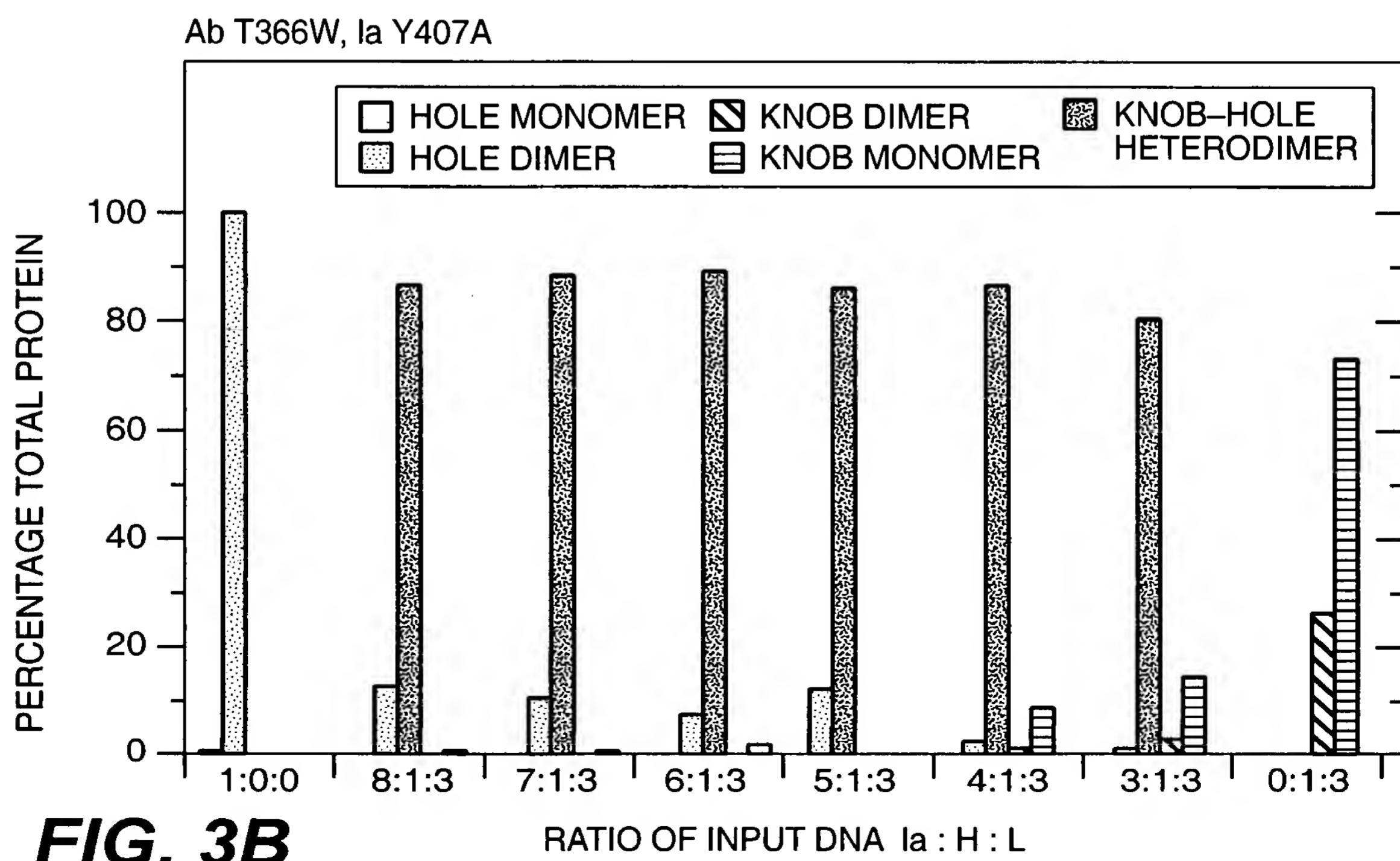


FIG. 3B

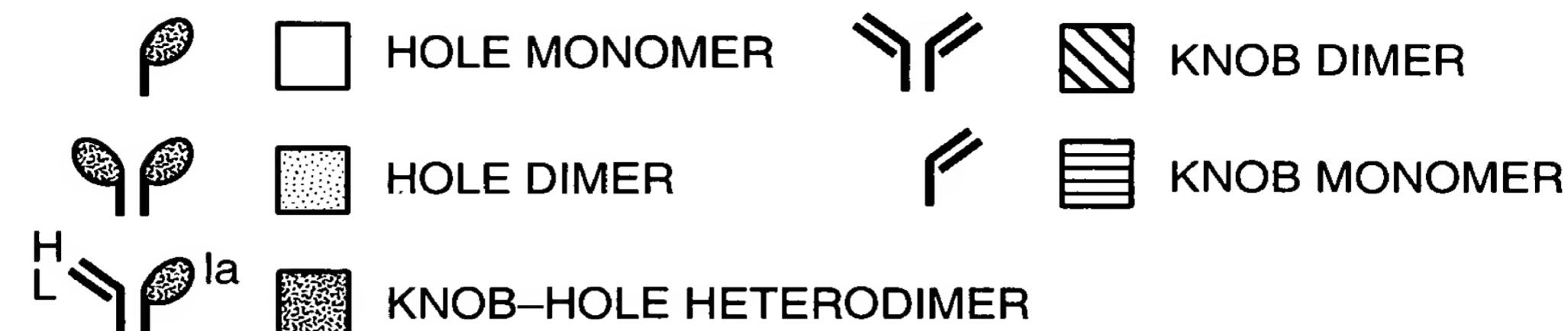


FIG. 3C

| | | | | | |
|----------------|---|-----|----|----|-------|
| 1 | 20 | abc | 30 | 40 | 50 |
| | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| Ax1.78 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| Rse. 23 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| IGER.MAT2C1G11 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| GCSFR.A4 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| Rse. 04 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| obr. 4 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| Rse. 20 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| Rse. 15 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| vegf.5 | QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV | | | | |
| | # ##### | | | | |
| | # ## | | | | |
| | CDR L2 | | | | |
| | CDR L1 | | | | |
| | CDR L3 | | | | |
| | 60 | 70 | 80 | 90 | a 100 |
| Ax1.78 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 14) | | | | |
| Rse. 23 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 15) | | | | |
| IGER.MAT2C1G11 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 16) | | | | |
| GCSFR.A4 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 17) | | | | |
| Rse. 04 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 18) | | | | |
| obr. 4 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 19) | | | | |
| Rse. 20 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 20) | | | | |
| Rse. 15 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 21) | | | | |
| vegf.5 | SNRFSGSKSGNTASLTISGLQAEDEADYYCSSLTRSTRVFGGGTKLTVL (SEQ ID NO: 22) | | | | |
| | # ##### | | | | |

FIG. 4

| | | |
|--|--|--------------------------------|
| V_H her3.18 10 20 <u>30</u> ab 40 50 a <u>QVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYEMN--WVTRQAPGKGLEWVSGTISGGSTYY</u> <u>* * * * * * * * *</u> | <u>EVQLVESGPCLVKPSQTLSLTCVSGGSTISSGGYYWSWIRQHPGKGLEWTIGYIY-YSGSTYY</u> <u>* * * * * * * * *</u> | <u>CDR H1</u> <u>CDR H2</u> |
|--|--|--------------------------------|

SGSGSGTDFTLTSSLQPDDFATYYCQQYSNYPLTFGGGTLKLEIK (SEQ ID NO: 25)
CDR L3

FIG 5

| | H1 | H2 | H3 | H4 | H5 | H6 | H7 | H8 | H9 | H10 | H11 |
|-----|----|-----|----|----|----|-----|----|----|-----|-----|-----|
| O1 | 49 | 47 | 51 | 81 | 60 | 48 | 76 | 51 | 100 | 62 | 51 |
| O2 | 84 | 79 | 88 | 50 | 48 | 99 | 48 | 88 | 48 | 45 | 88 |
| O3 | 83 | 82 | 85 | 51 | 50 | 95 | 49 | 85 | 49 | 46 | 85 |
| O4 | 47 | 50 | 51 | 83 | 77 | 48 | 65 | 51 | 73 | 64 | 51 |
| O5 | 49 | 47 | 51 | 81 | 60 | 48 | 76 | 51 | 100 | 62 | 51 |
| O6 | 83 | 79 | 86 | 50 | 50 | 99 | 47 | 86 | 48 | 45 | 86 |
| O7 | 81 | 100 | 86 | 51 | 49 | 80 | 48 | 86 | 47 | 44 | 86 |
| O8 | 81 | 100 | 86 | 51 | 49 | 80 | 48 | 86 | 47 | 44 | 86 |
| O9 | 81 | 100 | 86 | 51 | 49 | 80 | 48 | 86 | 47 | 44 | 86 |
| O10 | 83 | 79 | 85 | 50 | 49 | 98 | 46 | 85 | 48 | 45 | 85 |
| O11 | 83 | 80 | 87 | 50 | 49 | 99 | 47 | 87 | 48 | 45 | 87 |
| O12 | 81 | 100 | 86 | 51 | 49 | 80 | 48 | 86 | 47 | 44 | 86 |
| O13 | 49 | 47 | 51 | 81 | 60 | 48 | 76 | 51 | 100 | 62 | 51 |
| O14 | 50 | 50 | 54 | 95 | 67 | 49 | 76 | 54 | 75 | 62 | 54 |
| O15 | 82 | 79 | 85 | 49 | 48 | 97 | 46 | 85 | 47 | 44 | 85 |
| O16 | 84 | 80 | 87 | 50 | 49 | 100 | 47 | 87 | 48 | 45 | 87 |
| O17 | 45 | 44 | 47 | 65 | 62 | 45 | 62 | 47 | 62 | 100 | 47 |
| O18 | 50 | 51 | 50 | 75 | 79 | 50 | 63 | 50 | 66 | 62 | 50 |

01-018: ANTI-Ob-R ANTIBODY CLONES obr. 1, 11, 12, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 26, 3, 4, RESPECTIVELY.

H1-H11: ANTI-HER3 ANTIBODY CLONES her3.1, 3.10, 3.11, 3.12, 3.16, 3.18, 3.19, 3.22, 3.3, 3.4, 3.7, RESPECTIVELY.

FIG. 6